Abstract 262

Performance of the 17-gene Genomic Prostate Score test in men with prostate cancer managed with active surveillance: Results from the Canary Prostate Active Surveillance Study (PASS)

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BACKGROUND

- The 17-gene Genomic Prostate Score® (GPS™) test predicts adverse surgical pathology (AP) and recurrence in newly diagnosed low- and intermediate-risk prostate cancer (PCa) treated with immediate surgery.
- Studies of the performance of GPS in men initially managed with active surveillance (AS) are limited.

METHODS

- Diagnostic biopsy tissue was obtained from 634 men enrolled at 8 sites in PASS between August 2008 and February 2016.
- The primary endpoint was time to AP (Gleason GG ≥3, ≥pT3a, or N1) in men who underwent radical prostatectomy (RP).
- The secondary endpoint was time to upgrade (any increase in Gleason GG) on surveillance biopsy.
- All diagnostic biopsies and RP specimens were centrally reviewed.
- Multivariate regression models for interval censored data were used to evaluate the association between time to AP and GPS result. Inverse probability of censoring weighting was applied to adjust for informative censoring.
- Association between GPS result and time to Gleason score upgrade on surveillance biopsy was evaluated using a Cox Proportional Hazards model.

RESULTS

- Diagnostic tissue blocks were obtained for 634 patients
  - 17 (3%) did not meet inclusion criteria
  - 174 (27%) had insufficient tumor to assay
- Valid GPS results were obtained for 432 men
  - Median follow-up 4.6 [IQR: 2.9-6.2] years
  - 167 upgraded at subsequent biopsy
- 101 men underwent RP with central pathology review
  - Median time to treatment of 2.1 [IQR: 1.3-4.3] years
  - 52 had AP at surgery

RESULTS

Characteristic	Enrolled thru Feb. 2016 (n=1041)	Available FFPE blocks (n=634)	with GPS (n=432)	RP (n=101)
Age (years)	63 (58, 67)	63 (59, 67)	63 (59, 67)	62 (43, 76)
Race				
Asian	25 (2%)	18 (3%)	12 (3%)	5 (5%)
Black	74 (7%)	36 (6%)	24 (6%)	5 (5%)
Other	11 (1%)	8 (1%)	6 (1%)	0
White	931 (89%)	572 (90%)	390 (90%)	91 (90%)
BMI (kg/m^2)	27 (25, 30)	27 (25, 30)	27 (25, 30)	27 (25, 30)
Year of diagnosis	2011 (2009, 2012)	2011 (2009, 2013)	2011 (2009, 2013)	2011 (2009, 2013)
Family history of PCa	284 (27%)	165 (26%)	109 (25%)	25 (25%)
T-stage				
T1	929 (89%)	573 (90%)	385 (89%)	91 (90%)
T2a	103 (10%)	56 (9%)	42 (10%)	10 (10%)
T2b,c	9 (1%)	5 (1%)	5 (1%)	0
Dx biopsy Gleason *				
GG 1	958 (92%)	584 (92%)	374 (87%)	81 (80%)
GG 2	77 (7%)	46 (7%)	58 (13%)	20 (20%)
GG 3	6 (1%)	4 (1%)	0	0
% positive biopsy cores	8.3 (8.3, 16.7)	10.0 (8.3, 16.7)	12.5 (8.3, 16.7)	16.7 (8.3, 21.4)
PSA (ng/ml)	5.0 (3.8, 6.5)	4.9 (3.8, 6.6)	4.8 (3.7, 6.5)	4.8 (4.1, 6.1)
Prostate size (cm^3)	43 (31, 59)	42 (31, 58)	40 (31, 57)	35 (26, 47)
PSA density (ng/cm^3)	0.11 (0.08, 0.16)	0.11 (0.08, 0.16)	0.11 (0.08, 0.15)	0.14 (0.10, 0.19)
NCCN risk group**				
Very low	470 (45%)	310 (49%)	202 (47%)	37 (37%)
Low	411 (39%)	228 (36%)	142 (33%)	39 (39%)
Intermediate	160 (15%)	96 (15%)	88 (20%)	25 (25%)

Table 1. Participant characteristics at diagnosis, recorded either as median (IQR) or n (%).
*Biopsy Gleason score for entire PASS cohort and available FFPE blocks by clinical site pathology report, and Gleason score of patients with GPS and RP by central review.
**NCCN risk group determined for entire PASS cohort and available FFPE blocks using Gleason score from clinical site review of diagnostic biopsy, and for patients with GPS and RP using Gleason score from central review.

	N = 432, 167 events		N = 395 dx with GG 1, 157 events	
Variable	Hazard Ratio (95% CI)	p value	Hazard Ratio (95% CI)	p value
GPS (per 20 units)	0.90 (0.66, 1.22)	0.48	0.96 (0.73, 1.32)	0.81
Log_2 PSA density	1.44 (1.21, 1.71)	<.001	1.45 (1.21, 1.72)	<.001
% positive cores	1.03 (1.02, 1.04)	<.001	1.04 (1.02, 1.05)	<.001
Year of diagnosis	1.13 (1.04, 1.23)	0.003	1.11 (1.03, 1.21)	0.010

Table 4. Multivariable analysis for time to biopsy upgrade.

	Time to AP (N = 101)		Time to biopsy upgrade (N = 432)	
Variable	HR (95% CI)	p-value	HR* (95 % CI)	p-value
GPS (per 20 units)	1.70 (1.01,3.26)	0.062	1.02 (0.75, 1.38)	0.93
Age (per year)	1.01 (0.95, 1.05)	0.84	1.00 (0.97, 1.02)	0.70
Nonwhite vs. white race	0.94 (0.26, 2.58)	0.98	1.12 (0.68, 1.85)	0.66
Gleason score 7 vs. 6	0.85 (0.34,1.77)	0.68	0.70 (0.37, 1.34)	0.29
% positive cores	1.02 (0.99, 1.05)	0.29	1.04 (1.02, 1.05)	<0.001
Log PSA	1.65 (0.79, 4.29)	0.21	1.14 (0.88, 1.46)	0.32
Log prostate size	0.61 (0.24,1.45)	0.29	0.44 (0.32, 0.61)	<0.001
PSA density < 0.15 ng/mL^2	0.52 (0.26, 0.95)	0.054	0.44 (0.32, 0.61)	<0.001
Log_2 PSA density	1.78 (1.14, 3.11)	0.017	1.52 (1.29, 1.79)	<0.001
Clinical stage T2 vs. T1	2.48 (0.92,13.80)	0.14	0.97 (0.59, 1.6)	0.92
BMI (kg/m2)	1.05 (0.96, 1.13)	0.24	1.04 (1.00, 1.07)	0.049
Family history of PCa	0.81 (0.38, 1.59)	0.57	1.12 (0.79, 1.59)	0.52
Diagnosis year (per year)	1.09 (0.98, 1.25)	0.15	1.14 (1.05, 1.24)	0.002

Table 2. Univariable hazard ratios (HRs) for association of variables at diagnosis with A.) time to adverse pathology (AP) in 101 men who had RP after a period of surveillance, and B.) time to biopsy upgrade in 432 men using AS.

Variable	HR[a] (95% CI)	p value
Model 1		
GPS (per 20 units)	1.96 (1.17, 4.28)	.030
Gleason 7 vs. 6	0.62 (0.24, 1.33)	.26
Model 2		
GPS (per 20 units)	1.83 (1.04, 3.62)	.046
PSA density <0.15 ng/mL^2	0.49 (0.23, 0.90)	.037
Model 3		
GPS (per 20 units)	1.61 (0.87, 2.98)	.12
Log_2 PSA density	1.76 (1.14, 3.24)	.021

Table 3. Multivariable models for time to AP (n = 101).

CONCLUSIONS

- In a cohort of men on AS, GPS was associated with time to AP when adjusted for diagnostic GG or dichotomous PSAD.
- GPS was not significantly associated with AP at surgery after adjustment for continuous PSAD, although a trend was seen, suggesting an association may be seen in a larger study.
- GPS was not associated with upgrading in surveillance biopsy.

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